CLAIMS

1. A Factor VII polypeptide comprising at least two substitutions relative to the amino acid sequence of SEQ ID NO:1, wherein said substitutions comprise: (i) a first substitution consisting of replacement of F374 with any other amino acid, and (ii) one or more substitutions consisting of replacement with any other amino acid of one or more amino acids selected from the group consisting of L305, S314, K157, K337, D334, S336, V158, E296, and M298.

2. The Factor VII polypeptide according to claim 1, wherein F374 is replaced with any other amino acid and K157 is replaced with any other amino acid.

3. The Factor VII polypeptide according to claim 1, wherein F374 is replaced with any other amino acid and K337 is replaced with any other amino acid.

4. The Factor VII polypeptide according to claim 1, wherein F374 is replaced with any other amino acid and D334 is replaced with any other amino acid.

5. The Factor VII polypeptide according to claim 1, wherein F374 is replaced with any other amino acid and S336 is replaced with any other amino acid.

6. The Factor VII polypeptide according to claim 1, wherein F374 is replaced with any other amino acid and V158 is replaced with any other amino acid.

7. The Factor VII polypeptide according to claim 1, wherein F374 is replaced with any other amino acid and E296 is replaced with any other amino acid.

8. The Factor VII polypeptide according to claim 1, wherein F374 is replaced with any other amino acid and M298 is replaced with any other amino acid.

9. The Factor VII polypeptide according to claim 1, wherein F374 is replaced with any other amino acid and L305 is replaced with any other amino acid.

10. The Factor VII polypeptide according to claim 1, wherein F374 is replaced with any other amino acid and S314 is replaced with any other amino acid.

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11. The Factor VII polypeptide according to claim 1, further comprising at least one additional substitution at an amino acid residue in the protease domain, wherein said residue has been replaced with any other amino acid.

12. The Factor VII polypeptide according to claim 11, wherein at the most 20 additional amino acids in the remaining positions in the protease domain have been replaced with any other amino acid.

13. The Factor VII polypeptide according to claim 11, wherein the additional substitution is at a residue corresponding to a position selected from 159-170 of SEQ ID NO:1.

14. The Factor VII polypeptide according to claim 11, wherein the additional substitution is at a residue corresponding to a position selected from 290-304 of SEQ ID NO:1.

15. The Factor VII polypeptide according to claim 14, wherein R304 has been replaced by an amino acid selected from the group consisting of Tyr, Phe, Leu, and Met.

16. The Factor VII polypeptide according to claim 11, wherein the additional substitution is at a residue corresponding to a position selected from 306-312 of SEQ ID NO:1.

17. The Factor VII polypeptide according to claim 16, wherein M306 has been replaced by an amino acid selected from the group consisting of Asp and Asn.

18. The Factor VII polypeptide according to claim 16, wherein D309 has been replaced by an amino acid selected from the group consisting of Ser and Thr.

19. The Factor VII polypeptide according to claim 11, wherein the additional substitution is at a residue corresponding to a position selected from 330-339 of SEQ ID NO:1.

20. The Factor VII polypeptide according to claim 11, wherein A274 has been replaced with any other amino acid.

21. The Factor VII polypeptide according to claim 20, wherein said A274 has been replaced with an amino acid selected from the group consisting of Met, Leu, Lys, and Arg.

22. The Factor VII polypeptide according to claim 1, wherein said K157 has been replaced by an amino acid selected from the group consisting of Gly, Val, Ser, Thr, Asn, Gln, Asp, and Glu.

23. The Factor VII polypeptide according to claim 1, wherein said K337 has been replaced by an amino acid selected from the group consisting of Ala, Gly, Val, Ser, Thr, Asn, Gln, Asp, and Glu.

24. The Factor VII polypeptide according to claim 1, wherein said D334 has been replaced by an amino acid selected from the group consisting of Gly and Glu.

25. The Factor VII polypeptide according to claim 1, wherein said S336 has been replaced by an amino acid selected from the group consisting of Gly and Glu.

26. The Factor VII polypeptide according to claim 1, wherein said V158 has been replaced by an amino acid selected from the group consisting of Ser, Thr, Asn, Gln, Asp, and Glu.

27. The Factor VII polypeptide according to claim 1, wherein said E296 has been replaced by an amino acid selected from the group consisting of Arg, Lys, Ile, Leu and Val.

28. The Factor VII polypeptide according to claim 1, wherein said M298 has been replaced by an amino acid selected from the group consisting of Lys, Arg, Gln, and Asn.

29. The Factor VII polypeptide according to claim 1, wherein said L305 has been replaced by an amino acid selected from the group consisting of Val, Tyr and Ile.

30. The Factor VII polypeptide according to claim 1, wherein said S314 has been replaced by an amino acid selected from the group consisting of Gly, Lys, Gln, and Glu.

31. The Factor VII polypeptide according to claim 1, wherein said F374 has been replaced by an amino acid selected from the group consisting of Pro and Tyr.

32. The Factor VII polypeptide according to claim 31, wherein said F374 has been replaced by Tyr.

33. The Factor VII polypeptid according to claim 1, wherein said Factor VII polypeptide is human Factor VII.

34. The Factor VII polypeptide according to claim 1, wherein the ratio between the activity of said Factor VII polypeptide and the activity of the native Factor VIIa polypeptide shown in SEQ ID NO:1 is at least about 1.25.

35. The Factor VII polypeptide according to1, which is F374Y/L305V-FVII.

36. The Factor VII polypeptide according to claim 1, which is F374Y/L305V/S314E/K337A-FVII.

37. The Factor VII polypeptide according to claim 1, which is F374Y/L305V/S314E-FVII.

38. The Factor VII polypeptide according to claim 1, which is F374Y/L305V/K337A-FVII.

39. A polynucleotide construct encoding a Factor VII polypeptide according to claim 1.

40. A host cell comprising the polynucleotide construct according to claim 39.

41. The host cell according to claim 40, wherein the cell is selected from the group consisting of CHO cells , HEK cells and BHK cells.

42. A method for producing a Factor VII polypeptide, the method comprising cultivating a cell as defined in claim 40 in an appropriate growth medium under conditions allowing expression of the polynucleotide construct and recovering the resulting polypeptide from the culture medium.

43. A pharmaceutical composition comprising a Factor VII polypeptide as defined in claim 1; and, optionally, a pharmaceutically acceptable carrier.

44. A method for the treatment of bleeding disorders or bleeding episodes in a subject or for the enhancement of the normal haemostatic system, the method comprising administering a therapeutically or prophylactically effective amount of a Factor VII polypeptide comprising at least two substitutions relative to the amino acid sequence of SEQ ID NO:1, wherein said

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substitutions are (i) replacement of F374 with any other amino acid, and (ii) replacement with any other amino acid of one or more amino acids selected from the group consisting of L305, S314, K157, K337, D334, S336, V158, E296, and M298; to a subject in need thereof.